510(k) Summary

MAR - 5 2010

This summary of 510(k) safety and effectiveness information is supplied in accordance with the requirements of SMDA 1990 and 21 CFR 807.92.

The assigned 510 (k) number is k090123

Date: March 5, 2010

Submitted by:

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Trade Name:

Neonatal Biotinidase kit

Common Name:

Neonatal Biotinidase kit

Classification Name:

System, Test, Biotinidase (21 CFR 862.1118/ Product Code NAK)

Predicate device:

Astoria-Pacific SPOTCHECK® Biotinidase 50-Hour Reagent Kit, (K010844)

Device Description:

Biotinidase is found in the blood sample itself. Filter paper disks from newborn dried blood spot samples, calibrators and controls are punched into the wells of a microplate. When biotin substrate reagent containing biotin 6-aminoquinoline (6-AQ) is added to a well containing a punched dried blood spot, the reagent extracts and reconstitutes the proteins and enzymes in the spot. The biotinidase enzyme in the sample cleaves the substrate to biotin and fluorescent 6-AQ The addition of the ethanol stops the reaction and precipitates the proteins to cover the bottom of the well and the extracted spot. The fluorescent product (6-AQ) formed during the reaction is measured with a fluorometer. The biotinidase activity is defined against a calibration curve. The biotinidase activity of the sample is

determined by comparing the fluorescence intensity of the sample to a calibration curve.

Intended Use: The Neonatal Biotinidase kit is intended for the semi-quantitative determination of biotinidase activity in blood specimens dried on filter paper as an aid in screening newborns for biotinidase deficiency.

Device Comparison:

Comparison of the PerkinElmer Neonatal Biotinidase kit with the predicate device.

Parameter	Neonatal Biotinidase kit	Predicate Device
Intended Use	The **Neonatal Biotinidase kit** is intended for the semi-quantitative determination of biotinidase activity in blood specimens dried on filter paper as an aid in screening newborns for biotinidase deficiency.	The **Astoria-Pacific® SPOTCHECK Biotinidase 50 Hour Reagent Kit (k010844)** is intended for the semi-quantitative determination of biotinidase, EC 3.5.1.12, activity in dried whole blood spots using the Astoria-Pacific SPOTCHECK® Analyzer. Measurement of biotinidase activity is primarily for the diagnosis and treatment of biotinidase deficiency in newborns. This method is intended for in vitro diagnostic use to aid in screening for decreased levels of biotinidase activity and not for monitoring purposes.
Specimen type	Whole blood specimen spotted on filter paper	Same
Assay Technology	Enzymatic	Same
Kit content	Calibrators and enzymatic reagents. (additionally includes kit controls and microtiter plates)	Same
Interpretation of results	Calibration curve	Same
Test Principle	1-step enzymatic assay were the biotinidase in the sample cleaves the substrate biotin 6-aminoquinoline generating a fluorescent 6-aminoquinoline product.	2-step assay were biotinidase releases p-Aminobenzoic acid (PABA) from biotinyl-p-aminobenzoate. The PABA is diazotized and coupled to a napthol derivative to form a purple chromophore.

Parameter	Neonatal Biotinidase kit	Predicate Device
Detection technique	Fluorometric	Colorimetric
Instrumentation requirement	Fluorometer with excitation central wavelength of 355 nm and the emission central wavelength of 460 nm	Astoria-Pacific SPOTCHECK® Analyzer
Screening Outcome	Normal and Deficient	Normal, Partial Deficient and Profound Deficient
Measuring Unit	U	ERU
Calibrator Matrix	Dried Blood Spots prepared from porcine blood.	Liquid standards. PABA stock standard. 1.0 mM p-Aminobenzoic acid diluted with Tris Buffer.
Calibrator Levels	Six levels, ready to use 10 U 30 U 130 U 180 U 250 U 350 U	Six levels to be prepared from PABA stock standard 0 ERU 5 ERU 25 ERU 50 ERU 100 ERU 200 ERU
Kit controls	Included in the kit. Dried blood spots prepared from human blood. Normal 275 U Abnormal 50 U	Provided separately
Analytical sensitivity/Lower limits of detection	Limit of Blank = 12 U Limit of Detection = 16 U	Sensitivity = 1 ERU
Linearity	16 to 390 U	Not defined in predicate labeling
Measuring Range	16 to 350 U	Not defined in predicate labeling
Expected values	Normal Population Range: 31.5 – 388 U Mean: 163.8 U Median: 160.9 U	Normal Population Range: 19 to 121 ERU Average: 54 ERU

Parameter	Neonatal Biotinidase kit	Predicate Device
Interference	Neonate albumin levels above normal (2.8 to 4.4 g/dL) can interfere with this test by increasing biotinidase activity. This could result in the misclassification of a patient with a biotinidase result near the cut-off value as 'normal' when in fact, the patient should be classified as 'deficient'. A patient with known or clinically suspected elevated blood albumin concentration should be screened with an alternative method and confirmed according to local requirements for follow-up testing. Kanamycin sulphate, glutathione, sulfamethoxazole, sulfisoxazole, and trimethoprim can interfere with this test by increasing biotinidase activity. This could result in the misclassification of a patient with a biotinidase result near the cut-off value as 'normal' when in fact, the patient should be classified as 'deficient'. Patients or mothers known to have received kanamycin sulphate, glutathione, sulfamethoxazole, sulfisoxazole or trimethoprim should be screened with an alternative method and confirmed according to local requirements for follow-up testing. Gammaglobulin (1.8 g/dL at biotinidase activity level of 55 U and 1.5 g/dL at biotinidase activity levels of 80 U and 160 U) caused a decrease in biotinidase activity. This could result in a false positive result (biotinidase deficient) in normal patients with biotinidase	Sulfonamides react with color developing reagents. Phenytoin, ampicillin, gentamycin sulfate, vitamin K, penicillin G potassium, kanamycin sulphate, adrenocorticotropic hormone, valproic acid and sodium phenobarbital do not interfere at therapeutic concentrations. Samples spiked with up to 2.5 g/dL of combined albumin and globulin do not interfere as protein added above that level increased the response. Samples spiked with up to 100 mg/dL hemoglobin showed no interference. Samples spiked with up to 250 mg/dL of lipids showed no interference. Lipids added above that level decreased the response.

	values near the cut-off value. However, no interference was observed with gammaglobulin (6 g/dL) at a biotinidase activity level of 20 U. Triglycerides (Intralipid at 150 mg/dL for biotinidase activity levels of 55 U and 80 U, 300 mg/dL at biotinidase activity of 20 U and 400 mg/dL at biotinidase activity of 160 U) caused a decrease in biotinidase activity. This could result in a false positive result (biotinidase deficient) in normal patients with biotinidase values near the cut-off value. Biotin (500 ng/dL) at biotinidase activity level of 55 U caused a decrease in biotinidase activity. This could result in a false positive result (biotinidase deficient) in normal patients with biotinidase values near the cut-off value. Ampicillin (0.56 mg/dL), penicillin G potassium (18.75 mg/dL), sodium phenobarbital (5.5 mg/dL), and phenytoin (1.88 mg/dL) at biotinidase activity level of 160 U caused an increase in response, whereas no interference was observed at biotinidase levels of 20 U, 55 U and 80 U. Valproic acid (25 mg/dL) at biotinidase activity levels of 80 U and 160 U caused an increase in response, whereas no interference was observed at biotinidase activity levels of 20 U and 55 U. The following substances were found not to interfere at the concentrations indicated; adreno-	

corticotropic hormone (15 ng/dL), ampicillin (2.8 mg/dL for biotinidase activities of 20 U, 55 U and 80 U), ascorbic acid (3 mg/dL), biotin (500 ng/dL for biotinidase activities of 20 U, 80 U and 160 U), conjugated bilirubin (30 mg/dL), unconjugated bilirubin (20 mg/dL), EDTA (1 g/dL), gentamicin sulphate (0.5 mg/dL), hemoglobin (200 mg/dL), heparin (37.5 mg/dL), penicillin G potassium (25 mg/dL at biotinidase activities of 20 U, 55 U and 80 U), phenytoin (2.5 mg/dL for biotinidase activities of 20 U, 55 U and 80 U), sodium phenobarbital (5.5 mg/dL for biotinidase activities of 20 U, 55 U and 80 U) and vitamin K1 (0.2 mg/dL).

Precision

Precision

Within-Run, Within-Lot and Total Precision

Sample mean (U)	23	54	75	95	144	287
n	108	108	108	108	108	108
Min (U) measured	17	44	50	71	112	217
Max (U) measured	29	72	97	121	175	358
Within run SD	1.4	4.4	5.9	7.9	10	21
Within run CV%	6.3	8.2	7.9	8.3	7.2	7.4
Within lot SD	2	5.2	7.8	10	14	30
Within lot CV%	8.8	9.7	10	11	9.8	11
Total SD	2.3	5.5	8.4	11	16	35
Total CV%	9.9	10	11	11	11	12

Precision

Within-Run and Total Precision

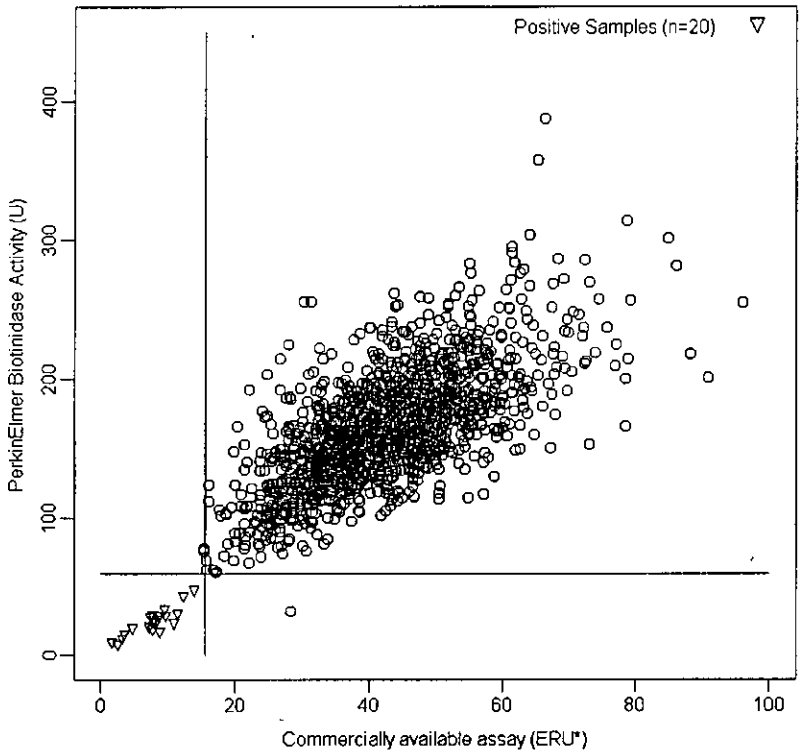
	Deficient (Profound)	Partial Activity	Normal
n	32	44	44
Average BTD* activity (ERU)	0.54	14.6	3.2
Within-Run Precision, S_{WR}			
SD	0.09	0.47	3.8
CV%	17	3.2	4.7
Total Precision, S_T			
Average	0.54	14.6	79.6
SD	0.30	0.94	4.6
CV%	56	6.4	5.8

*Biotinidase

Method Comparison

The method comparison was determined in accordance with NCCLS document EP9-A2.

The PerkinElmer Neonatal Biotinidase kit was compared with the Astoria-Pacific Biotinidase 50-Hour Reagent kit (k010844). The samples used in the study included 1516 newborn dried blood spot specimen representing US population analyzed as singlicates with the Neonatal Biotinidase kit and with a commercially available assay. The samples consisted of 1496 routine screening specimens and 20 retrospective specimens diagnosed positive for biotinidase deficiency. The cutoffs were determined according to each method's respective labeling (30% of mean ±2 SD for the Neonatal Biotinidase and 37% of the mean for predicate). All of the 20 clinically confirmed deficient samples were positive by both methods. The observed activities are shown in the following figure.



The evaluation data (n = 1516) with routine and known positive samples. The routine samples are illustrated with (o) and the known positive samples with (▽). The cut-offs are presented with solid lines.

* Enzyme response unit (ERU)

The screening summaries according to each method's respective labeling are presented in the tables below. The screening positives (+) are samples < cut-off and the screening negatives (–) are samples ≥ cut-off.

Screening result Commercially available kit	Screening result PerkinElmer kit	Total subjects	Diagnosed biotinidase deficiency	No diagnosed biotinidase deficiency
+	+	20	20	0
+	-	2	0	2
-	+	1	0	1
-	-	1493	0	1493
Total		1516	20	1496

	Commercially available kit		Total
PerkinElmer kit	Positive (< 15.7 ERU)	Negative (≥ 15.7 ERU)	
Positive (<58.5U)	20	1	21
Negative (≥58.5U)	2	1493	1495
Total	22	1494	1516

The positive percent agreement was 90.9% (20/22) and the overall percent agreement was 99.8% ((20+1493)/1516).

DEPARTMENT OF HEALTH & HUMAN SERVICES

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Division of PerkinElmer, Inc.
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MAR 0 5 2010

Re: k090123
Trade/Device Name: PerkinElmer Neonatal Biotinidase Kit
Regulation Number: 21 CFR §862.1118
Regulation Name: Biotinidase Test System
Regulatory Class: Class II
Product Code: NAK, JIT, JJX
Dated: February 9, 2010
Received: February 16, 2010

Dear Ms. Taylor:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820).

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Office of *In Vitro* Diagnostic Device Evaluation and Safety at (301) 796-5450. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding postmarket surveillance, please contact CDRH's Office of Surveillance and Biometric's (OSB's) Division of Postmarket Surveillance at (301) 796-5760. For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-5680 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Courtney C. Harper, Ph.D.
Director
Division of Chemistry and Toxicology
Office of *In Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and Radiological Health

Enclosure

Indication for Use

510(k) Number (if known): K090123

Device Name: PerkinElmer Neonatal Biotinidase Kit

Indication For Use: The Neonatal Biotinidase kit is intended for the semi-quantitative determination of biotinidase activity in blood specimens dried on filter paper as an aid in screening newborns for biotinidase deficiency.

Prescription Use X And/Or Over the Counter Use ___.
(21 CFR Part 801 Subpart D) (21 CFR Part 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE; CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostic Device Evaluation and Safety (OIVD)

Carol C Benson

Division Sign-Off
Office of In Vitro Diagnostic Device
Evaluation and Safety

510(k) K090123